Amendments to the Claims:

1. (Original) A method of changing a functional surface binding specificity of a PAS domain, wherein the PAS domain is predetermined, prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, the method comprising the steps of:

introducing into the hydrophobic core of the PAS domain a foreign ligand of the PAS domain; and

detecting a resultant change in the functional surface binding specificity of the PAS domain.

2. (Original) A method according to claim 1, wherein the binding specificity is a change in intermolecular binding affinity of the PAS domain.

3. (Original) A method according to claim 1, wherein the binding specificity is a change in intramolecular binding affinity of the PAS domain.

4. (Original) A method according to claim 1, wherein the binding specificity is manifested as a change in kinase activity or specificity.

5. (Original) A method according to claim 1, wherein the binding specificity is manifested as a change in channel patency or specificity.

6. (Original) A method according to claim 1, wherein the PAS domain is expressed by and within a host cell or animal.

7. (Original) A method according to claim 1, wherein the PAS domain is expressed by and within a host cell or animal, and the ligand is foreign to the host.

8. (Original) A method according to claim 1, wherein the PAS domain is expressed by and within a host cell or animal, and the change is detected indirectly as a change in host cell or animal physiology precorrelated with the change in binding specificity.

9. (Original) A method according to claim 4, wherein the PAS domain is expressed by and within a host cell or animal, and the change is detected indirectly as a change in host cell or animal physiology precorrelated with the change in binding specificity.

10. (Original) A method according to claim 5, wherein the PAS domain is expressed by and within a host cell or animal, and the change is detected indirectly as a change in host cell or animal physiology precorrelated with the change in binding specificity.

11. (Original) A method according to claim 1, wherein the PAS domain is selected from the group consisting of PAS kinase PAS A, NPAS2 PAS A, HIF2a PAS B, HIF1a PASB, ARNT PAS B and human ether-a-go-go related gene (HERG) N-terminal PAS.

12. (Original) A method according to claim 1, wherein the PAS domain is part of a larger protein selected from the group consisting of PAS kinase, NPAS2, HIF2a, ARNT, HIF1a and HERG protein.

13. (Original) A method according to claim 8, wherein the PAS domain is part of a larger protein selected from the group consisting of PAS kinase, NPAS2, HIF2a, ARNT, HIF1a and HERG protein.

14. (Original) A method according to claim 9, wherein the PAS domain is part of a larger protein selected from the group consisting of PAS kinase, NPAS2, HIF2a, ARNT, HIF1a and HERG protein.

15. (Original) A method according to claim 10, wherein the PAS domain is part of a larger protein selected from the group consisting of PAS kinase, NPAS2, HIF2a, ARNT, HIF1a and HERG protein.

16. (New) A method according to claim 1, wherein the PAS domain is PAS kinase PAS A.

17. (New) A method according to claim 4, wherein the PAS domain is PAS kinase PAS A.

18. (New) A method according to claim 9, wherein the PAS domain is PAS kinase PAS A.

19. (New) A method according to claim 1, wherein the PAS domain is part of PAS kinase.

20. (New) A method according to claim 4, wherein the PAS domain is part of PAS kinase.